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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/773,084 | 02/05/2004 | Xiaojian Zhao | C0989.70049US01 | 3297 |

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Maria A. Trevisan
Wolf, Greenfield & Sacks, P.C.
600 Atlantic Avenue
Boston, MA 02210

| EXAMINER | |
|---|---|
| WHISENANT, ETHAN C | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1634 | |

DATE MAILED: 05/16/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/773,084 | ZHAO ET AL. | |
| | Examiner | Art Unit | |
| | Ethan Whisenant, Ph.D. | 1634 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *12 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *137-139,141,142,144,148,149 and 164-175* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *137-139,141,142,144,148,149,164-170 and 172-175* is/are rejected.

7)☒ Claim(s) *171* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 February 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

**NON-FINAL ACTION**

1. The applicant's Preliminary Amendment filed 12 JAN 05 has been entered. Following the entry of the Preliminary Amendment, **Claim(s) 137-139,141-142, 144, 148-149 and 164-175** is/are pending.

**35 USC § 102**

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that may form the basis for rejections set forth in this Office action:

> A person shall be entitled to a patent unless --
>
> **(a)** the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> **(b)** the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> **(e)** the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.
> or
> **(e)** the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

3. The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

**Claim Rejections under 35 USC § 102**

**4.** **Claim(s) 137-139, 141-142, 144, 148, 165-170 and 175** is/are rejected under 35 U.S.C. 102(b) as being anticipated by Chen et al. [Genome Research (1998)].

Chen et al. (1998) teach a method for detecting a mutant polymer comprising all of the limitations recited in Claims 137-139, 141-142, 144, 148, 165-170 and 175. As regards the embodiment recited in Claim 13, please note that the polymer in Chen et al. is single stranded at that stage of the assay when the ligation probes anneal. As regards the phrase "molecular beacon" in Claim 28, the examiner asserts that the probes used by Chen et al. can be termed "molecular beacons." Please note that while the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. *In re Van Guens*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

**35 USC § 103**

**5.** The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> **(a)** A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

**6.** This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligations under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

**CLAIM REJECTIONS UNDER 35 USC § 103**

**7. Claim(s) 172-173** is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al. [Genome Research (1998)] as applied against Claim 137 above and further in view of Sokol et al. [PNAS (1998)].

Chen et al. teach a method for detecting a mutant polymer comprising all of the limitations recited in Claim 172-173 except these authors do not teach detecting a mutant polymer wherein the mutant polymer is fixed to the solid support in a random orientation or a non-continuous manner. However, Sokol et al. do teach detecting DNA• RNA hybridization in living cells using FRET and fluorescence microscopy (i.e. direct imaging) wherein the mutant polymer is fixed to the solid support in a random orientation or a non-continuous manner. Therefore, absent an unexpected result it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the method of detection taught by Chen et al. wherein the target polymer is fixed to the solid support in a random orientation or a non-continuous manner. Please note that substitution of one well known method/reagent with known properties for a second well known method/reagent with well known properties would have been *prima facie* obvious to the ordinary artisan at the time of the invention in the absence of an unexpected result. As regards the motivation to make the substitution recited above, the motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose.

**8. Claim(s) 149, 170 and 174** is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al. [Genome Research (1998)] as applied against Claim 137 above and further in view of Rigler et al. [WO03/076655 (2003)].

Chen et al. teach a method for detecting a mutant polymer comprising all of the limitations recited in Claim 149 except these authors do not teach detecting a mutant polymer wherein a laser is used to excite a donor FRET flurophore and then detect a signal from a acceptor flurophore. However, Rigler et al. do teach detecting a mutant polymer which utilizes a laser to excite a donor FRET flurophore and then detects a signal from a acceptor flurophore. Therefore, absent an unexpected result it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the method of detection taught by Chen et al. wherein the target polymer is detected using a laser to excite the donor flurophore. Please note that substitution of one well known method/reagent with known properties for a second well known method/reagent with well known properties would have been *prima facie* obvious to the ordinary artisan at the time of the invention in the absence of an unexpected result. As regards the motivation to make the substitution recited above, the motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their

expected results when combined for their common known purpose.

Chen et al. teach a method for detecting a mutant polymer comprising all of the limitations recited in Claim 170 except these authors do not explicitly teach detecting a mutant polymer wherein the first and second detectable labels are provided as molecular beacons (i.e. single stranded oligonucleotides that become fluorescent when they bind to perfectly complementary nucleic acids. However, Rigler et al. do teach using molecular beacon probes to detect a mutant polymer which utilizes a laser to excite a donor FRET flurophore and then detects a signal from a acceptor flurophore. Therefore, absent an unexpected result it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the method of detection taught by Chen et al. wherein the target polymer is detected using molecular beacon type probes. Please note that substitution of one well known method/reagent with known properties for a second well known method/reagent with well known properties would have been *prima facie* obvious to the ordinary artisan at the time of the invention in the absence of an unexpected result. As regards the motivation to make the substitution recited above, the motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose.

**Claim 174** is drawn to an embodiment of Claim 137 wherein the binding of the mutant-specific unit specific marker and polymer-specific unit specific marker to the polymer is determined by confocal detection.

Rigler et al. teach this limitation, see, at least for example, the IT portion of the English language CAplus summary of the German language WO02/072885 document, wherein it is taught that Rigler et al. use Confocal laser scanning microscopy to detect the hybridization of pairs of stem-loop forming probes.

**9. Claim(s) 139** lacks an inventive step under PCT Article 33(3) as being obvious over Chen et al. [Gemome Research (1998)] as applied against Claims 1 and 3 above and further in view of Stoughton et al. [US 6,673,536 (2004)].

Chen et al. teach a method for detecting a mutant polymer comprising all of the limitations recited in Claim 139 except these authors do not explicitly teach detecting a mutant polymer which mutant polymer is RNA. However, as evidenced by Stoughton et al. it was well known in the art at the time of the invention that one could detect mutant mRNA. Therefore, absent an unexpected result it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the method of detection taught by Chen et al. wherein the target polymer examined is mRNA. Please note that substitution of one well known method/reagent with known properties for a second well known method/reagent with well known properties would have been *prima facie* obvious to the ordinary

artisan at the time of the invention in the absence of an unexpected result. As regards the motivation to make the substitution recited above, the motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose.

**10. Claim(s) 164** lacks an inventive step under PCT Article 33(3) as being obvious over Chen et al. [Gemome Research (1998)] as applied against Claims 137 above and further in view of Parker et al. [US 5,565,323 (1996)].

Chen et al. teach a method for detecting a mutant polymer comprising all of the limitations recited in Claim 164 except these authors do not explicitly teach detecting a mutant polymer wherein the method further comprises a column purification step. However, as evidenced by Parker et al., it was common place at the time of the invention to use column purification to purify oligonucleotide primers and probes. Therefore, absent an unexpected result it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the method of detection taught by Chen et al. wherein the primers used by Chen et al. were purified using a column purification step. Please note that substitution of one well known method/reagent with known properties for a second well known method/reagent with well known properties would have been *prima facie* obvious to the ordinary artisan at the time of the invention in the absence of an unexpected result. As regards the motivation to make the substitution recited above, the motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose.

## CLAIM OBJECTIONS

**11. Claim(s) 171** is /are objected to as being dependent upon a rejected base claim, but would appear to be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

## CONCLUSION

**12. Claim(s) 137-139,141-142, 144, 148-149 and 164-175** is/are rejected and/or objected to for the reason(s) set forth above.

**13.** Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ethan Whisenant, Ph.D. whose telephone number is (571) 272-0754. The examiner can normally be reached Monday-Friday from 8:30AM -5:30PM EST or any time via voice mail. If repeated attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached at (571) 272-0745.

The fax number for this Examiner is (571) 273-0754. Before faxing any papers please inform the examiner to avoid lost papers. Please note that the faxing of papers must conform with the Notice to Comply published in the Official Gazette, 1096 OG 30 (November 15, 1989).

ETHAN WHISENANT
PRIMARY EXAMINER
Art Unit 1634

## SEARCH NOTES

18 APR 05

**Databases searched: USPATFULL, USPGPUBS and EUROPATFULL via EAST, CAplus, Medline**

Search terms:

Inventor(s) : e.g. Zhao X?/au

Oligonuc$ or probe? or primer?

Hybridization

RNAor mRNA

SNP$

FRET